REMARKS

The present communication responds to the Office Action dated May 16, 2007. In that Office Action, the Examiner rejected each of the pending claims. Reconsideration and allowance are requested at least for the reasons discussed below.

Rejections Under 35 U.S.C. § 103

Independent Claim 1 is not obvious over '432 in view of the '104 patent

Claims 1, 2, 6, 9-11, 13-18, and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,977,432 ("the '432 patent") in view of U.S. Patent No. 5,976,104 ("the '104 patent").

Claim 1 recites a process for inactivating and/or reducing pathogens from tissue comprising, in part, "centrifuging the tissue in a centrifuge with a flowing pathogen solvent reducing solution wherein the solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging."

The '432 patent, in contrast, does not disclose each of the elements of claim 1. Particularly, the '432 patent does not disclose, at least, "wherein [pathogen solvent reducing] solution is flowed continuously to and away from the centrifuge containing the tissue during centrifuging," as recited by claim 1. The '432 patent discloses a multi-step batch process for removal of bone marrow from the interstitial lumen and cancellous bone space through creation of a centrifugational force. *The '432 patent*, col. 4, ll. 21-25. The process begins with a series of pre-clean or incubation procedures, including one or more of lavaging, soaking, sonicating, and agitating the cut bone grafts in cleaning solutions. *The '432 patent* , col. 7, ll. 52 – 61. The bone graft is then transferred in a hydrogen peroxide solution to a centrifuge tube and centrifuged for a specified period. The '432 *patent*, col. 12, ll. 20-22. Subsequently, the bone grafts are removed from their centrifuge tubes and again incubated and/or cleaned by one or more of lavaging, soaking, sonicating, and agitating the cut bone grafts in cleaning solutions. *The '432 patent*, col. 7, ll. 52 – 61. The bone grafts are then subjected to a series of washing solutions before

experiencing a final centrifuging process. *The '432 patent*, col. 12, ll. 34-62. In sum, the '432 patent discloses a series of batch cleaning/incubating/washing procedures wherein a vast majority involve the treatment of a bone graft outside of a centrifuge. Accordingly, the '432 patent does not disclose, teach, or suggest "wherein [pathogen solvent reducing] solution is flowed continuously to and away from the centrifuge containing the tissue during centrifuging," as recited by claim 1. Notably, the Examiner concedes as much in the Office Action of May 16, 2007 (the "Office Action").

The Examiner attempts to remedy the deficiencies of the '432 patent by combining it with the teachings of the '104 patent. The '104 patent is directed to a method of removing bone marrow from the luminal and cancellous bone spaces in essentially intact bone grafts. *The '104 patent*, col. 1, ll. 50-52. In the method of the '104 patent, a bone is prepared for attachment to a solvent line by drilling a small hole approximately midway between its proximal and distal ends. *The '104 patent*, col. 5, ll. 36-39. The bone is then attached to the solvent line and placed into a solvent solution in a sterile cleaning container. *The '104 patent*, col. 5, ll. 40-43. Solvents may then be drawn using a negative pressure flow or flushed using positive pressure flow, through the bone. *The '104 patent*, col. 6, ll. 5-7. The '104 patent does not disclose, teach, or suggest an alternative method of removing bone marrow nor does it disclose, teach, or suggest that its method may be employed in conjunction with an alternative method. Specifically, the '104 patent does not disclose, teach, or suggest that the method may be used in conjunction with a centrifuge.

The '104 patent does not remedy the disclosure deficiencies of the '432 patent at least because the combination is improper. The Examiner is respectfully reminded that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977 (CA Fed. 1996) (cited with approval in *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727 (2007)). As support for the combination, the Examiner asserts

> "It would have been obvious to one of ordinary skill in the art at the time of the invention to provide a means to continuously introduce to and remove from the centrifuge of [the '432 patent] in order to monitor complete removal of bone marrow from the graft of [the '432 patent]. In fact, [the '432 patent] teaches that the

> purpose of centrifuging the bone graft is to remove the bone marrow from the graft (col. 3, lines 5-8) and that complete removal of the bone marrow from the graft can be monitored 'continually during the process' by measuring the absorbance of the solution. *Office Action*, page 3.

Applicants respectfully traverse the Examiner's reasoning at least because continually monitoring the degree to which bone marrow has been removed from a bone graft, as disclosed in the '432 patent, and the continuous flowing of solvent in a centrifuge, as recited in claim 1, are wholly unrelated concepts. As disclosed in the '432 patent, monitoring may include taking core samples of bone plugs, solubilizing bone marrow from a bone plug sample, visual inspection using an electron microscope, as well as visual inspection with the naked eye. *The '432 patent*, col. 11, ll. 1-9. Furthermore, much, if not all of the "monitoring" of the '432 patent occurs outside of the centrifuge. *The '432 patent*, col. 11, ll. 9-60. Accordingly, monitoring, as disclosed in the '432 patent, bears no connection to continuous flow of solvent in a centrifuge and does not teach or suggest the employment of continuous flow in a centrifuge.

Beyond the lack of rational or suggestion for making the '432 patent and the '104 patent combination, the combination of the '432 patent and the '104 patent further is improper at least because the '432 patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process:

> The use of more traditional flushing procedures to remove bone marrow involves the use of pressurized flow of solution as a rapidly moving stream which dislodges bone marrow by impact of the solvent on the bone graft. Such procedures tend to generate aerosols of tissue and solvent which can be hazardous to processing personnel. The present invention virtually eliminates this hazard. *The '432 patent,* col. 8, ll. 23-29.

The Examiner is respectfully directed to *Gillette Co. v. S.C. Johnson & Sons, Inc.*, 16 USPQ2d 1923 (Fed. Cir. 1990) where the Federal Circuit held that prior art which would "discourage" the ordinarily skilled artisan from attempting the claimed invention cannot validly support a rejection under 35 U.S.C. § 103. By disparaging the use of flowing solution in the art, the '432 patent has unequivocally discouraged the skilled artrisan from employing a flow of solution. Accordingly, a rejection under § 103 which attempts to

combine the '432 patent with any reference for the purpose of teaching flow of solution is clearly improper.

As still further support of nonobviousness, Applicants note that the '104 patent is incorporated in its entirety into the '432 patent specification. *The '432 patent*, col. 2, l. 64 – col. 3, l. 2. In other words, the '432 patent disclosed the recirculation method of the '104 patent and failed not only to disclose the combination, but also failed to teach or suggest that a recirculation method may be employed in its process. Rather, the '432 patent elected to explicitly teach away from the use of solution flow, continuous or otherwise, and to exclusively disclose and emphasize a batch cleaning process, much of it occurring outside of a centrifuge. Such an emphasis, especially in light of incorporation of the '104 patent, strongly teaches away from the continuous solution flow cleaning of a tissue in a centrifuge such as recited in ""wherein [pathogen solvent reducing] solution is flowed continuously to and away from the centrifuge containing the tissue during centrifuging" of claim 1.

In summary, the Applicants respectfully submit that the combination of the '432 patent and the '104 patent is improper. First, the Applicants respectfully submit that there is no reasonable rationale to combine the teachings of the '432 patent and the '104 patent, as advanced by the Examiner, except from using Applicants' invention as a template through hindsight reconstruction of Applicant's claims. Such hindsight reconstruction is impermissible. Second, even using hindsight, such combination is improper and would not be done because the '432 patent explicitly teaches away from the teachings of the '104 patent that the Examiner attempts to combine with the '432 patent. Third, the combination does not result in the claimed invention at least because, arguably, the teachings are already combined to the extent the inventors considered proper by incorporation by reference of the '104 patent into the '432 patent specification. The Applicants thus respectfully submit that claim 45 is in condition for allowance. Reconsideration and withdrawal of the rejection are requested.

Claims Depending From Claim 1 Are Patentable

Claims 2, 4, 6, 9-11, and 13-23 depend either directly or indirectly from claim 1 and incorporate all the limitations of claim 1. Accordingly, the Applicants respectfully submit that these claims are patentable at least for the reasons presented above. Reconsideration and withdrawal of the rejections are respectfully requested.

Independent Claim 38 is not obvious over the '432 patent in view of Morris

Claims 38 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '432 patent in view of Published International Application No. WO 01/58497 ("Morris").

Claim 38, as amended, recites a process for introducing a growth factor in animal tissue comprising, in part, centrifuging the tissue in a centrifuge in a liquid "wherein the liquid is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging."

The '432 patent, in contrast, does not disclose each of the elements of claim 38. Specifically, the '432 patent does not disclose "wherein the liquid is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging," as recited by claim 38, as amended. Not only does the '432 patent not disclose the use of solution flow during its process, as previously noted, the '432 patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process.

Morris does not remedy the deficiencies of the '432 patent. Rather, Morris teaches an apparatus for treating the interior of a fluid permeable workpiece by establishing a pulsatile flow of fluid using pressure differentials. More specifically, in the method of Morris, an end of a bone is placed in a first chamber and another end of the bone is placed in a second chamber. *Morris, page 12.* Alternating pressure cycles between the first chamber and second chamber is then provided to achieve a pulsatile type flow through the bone. *Morris, page 12.* Morris does not disclose, teach, or suggest continuously flowing a liquid. Accordingly, Morris does not disclose, teach, or suggest wherein a liquid is flowed continuously to and away from a centrifuge containing tissue during centrifuging.

Thus, neither the '432 patent nor Morris, alone or in combination, disclose, teach, or suggest, at least, centrifuging the tissue in a centrifuge in a liquid "wherein the liquid is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging," as recited by claim 38. The Applicants thus respectfully submit that claim 38 is in condition for allowance. Reconsideration and withdrawal of the rejection are requested.

Independent Claim 45 is not obvious over the '432 patent in view of the '933 patent

Claim 45 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '432 patent in view of U.S. Patent No. 5,730, 933 ("the '933 patent").

Claim 45, as amended, recites a process for providing infusion of a radiation protectant into tissue having a plurality of cavities comprising, in part, "centrifuging the tissue in a centrifuge with a solution ... wherein the solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging."

The '432 patent, in contrast, does not disclose each of the elements of claim 45. Specifically, the '432 patent does not disclose wherein the "solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging," as recited by claim 45, as amended. Not only does the '432 patent not disclose the use of solution flow during its process, as previously noted, the '432 patent explicitly teaches away from the use of solution flow, continuous or otherwise, during its process.

The '933 patent does not remedy the deficiencies of the '432 patent. The '933 patent teaches a method of sterilizing biologically active compounds with gamma or electron-beam radiation. *The '933 patent,* col. 3, ll. 3-10. Under the method of the '933 patent, following treatment with an extraneous protein and a free-radical scavenger to form a protected mixture, the mixture is irradiated under conditions that inactivate any pathogenic microorganisms. *The '933 patent,* col. 3, ll. 8-12. The '933 patent does not disclose continuously flowing a solution. Accordingly, the '933 patent does not disclose, teach, or suggest "centrifuging the tissue in a centrifuge with a solution ... wherein the solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging," as recited by claim 45, as amended.

Thus, neither the '432 patent nor the '933 patent, alone or in combination, disclose, teach, or suggest "centrifuging the tissue in a centrifuge with a solution ... wherein the solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging," as recited by claim 45, as amended. The Applicants thus respectfully submit that claim 45 is in condition for allowance. Reconsideration and withdrawal of the rejection are requested.

Rejections Under 35 U.S.C. § 102

Claims 25, 27, 30, 31, 44 and 46 are rejected under 35 U.S.C. § 102(b) as being anticipated by the '432 patent.

Independent Claim 25 is Not Anticipated by the '432 patent

Claim 25, as amended, recites a process for inactivating and/or reducing pathogens in bone tissue, comprising in part, centrifuging the tissue in a centrifuge with a pathogen solvent reducing solution wherein the pathogen solvent reducing solution is flowed continuously to and away from the centrifuge containing the tissue during the centrifuging.

As discussed above, and as conceded by the Examiner in the Office Action, the '432 patent does not disclose wherein a pathogen reducing solvent is flowed continuously to and away from a centrifuge containing tissue during centrifuging. Accordingly, the '432 patent does not disclose the invention of claim 25. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims Depending from Claim 25 are Patentable

Claims 27, 30-37, 39, and 44 depend either directly or indirectly from claim 25 and incorporate all the limitations of claim 25. Accordingly, the Applicants respectfully submit tht these claims are allowable at least for the reasons discussed above with respect to claim 25. Reconsideration and withdrawal of the rejections are respectfully requested.

Allowed Claims

Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants thank the Examiner for this allowance.

CONCLUSION

In light of the above, it is respectfully submitted that the present application is in condition for allowance. Reconsideration of the present application and a favorable response are respectfully requested.

This response is being submitted on or before October 16, 2007, with the required fee for a 2-month extension of time, making this a timely response. It is believed that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees or credit any overpayments to Deposit Account No. 04-1420.

If a telephone conference would be helpful in resolving any remaining issues, please contact the undersigned at (612) 492-6514.

Respectfully submitted,

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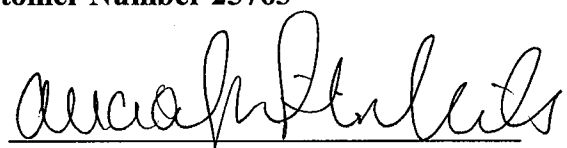
Date: October 16, 2007

By: 
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